



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/781,894

02/20/2004

Louis S. Kucera

053665-5012

4211

9629 7590 03/23/2010
MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

EXAMINER

ANDERSON, JAMES D

ART UNIT

PAPER NUMBER

1614

MAIL DATE

DELIVERY MODE

03/23/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/781,894 | Applicant(s) KUCERA ET AL. | |
| | Examiner JAMES D. ANDERSON | Art Unit 1614 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 February 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,6-8 and 39 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,6-8 and 39 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1614

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 2/26/2010, are acknowledged and entered. Claims 3-5 have been cancelled by Applicant. Claims 1-2, 6-8, and 39 are pending and under examination.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 2/26/2010 has been entered.

Response to Arguments

Any previous rejections and/or objections to claims 3-5 are withdrawn as being moot in light of Applicant's cancellation of the claims.

Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

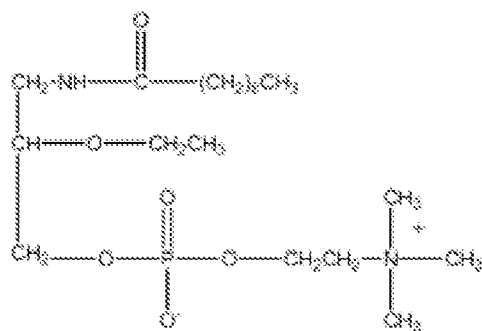
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Art Unit: 1614

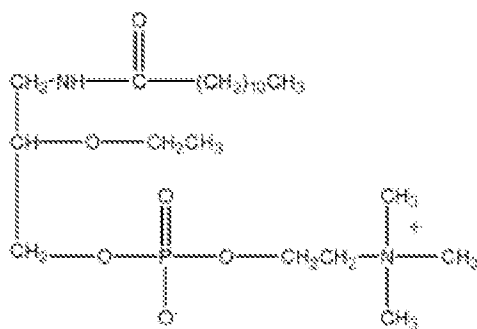
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 6-8, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Kucera *et al.*** (U.S. Patent No. 5,962,437; Issued Oct. 5, 1999; Filed Aug. 7, 1995) in view of **Kucera *et al.*** (U.S. Patent No. 3; Issued Jun. 23, 1998; Filed Jun. 6, 1995).

The instant claims recite methods of treating RSV infections comprising administering a compound having the formula

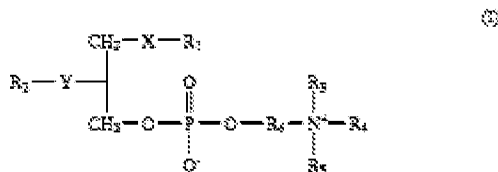


or



Kucera *et al.* teach methods of treating viral infections comprising administering to a subject a phospholipid or phospholipid derivative (Abstract). Such phospholipid derivatives are defined as compounds of Formula I:

Art Unit: 1614



In the compounds of Formula I, R_1 is a branched or unbranched, saturated or unsaturated C_6 to C_{16} alkyl group optionally substituted from 1 to 5 times with $-\text{OH}$, $-\text{COOH}$, oxo, amine, or substituted or unsubstituted aromatic; X is selected from the group consisting of NHCO , CH_2NCO , CONH , CONCH_3 , S , SO , SO_2 , O , NH , and NCH_3 ; R_2 is a branched or unbranched, saturated or unsaturated C_6 to C_{16} alkyl group optionally substituted from 1 to 5 times with $-\text{OH}$, $-\text{COOH}$, oxo, amine, or substituted or unsubstituted aromatic; Y is selected from the group consisting of NHCO , CH_2NCO , CONH , CONCH_3 , S , SO , SO_2 , O , NH , and NCH_3 ; R_3 is a branched or unbranched C_2 to C_6 alkyl group; and R_4 and R_5 are independently methyl or ethyl, or R_4 and R_5 together form an aliphatic or heterocyclic ring having five or six members and R_5 is methyl or ethyl. Preferred compounds include 1-dodecanamido-2-decyloxypropyl-3-phosphocholine, 1-dodecanamido-2-octyloxypropyl-3-phosphocholine, and 1-dodecanamido-2-dodecyloxypropyl-3-phosphocholine. The method is particularly preferred as a treatment to combat viral infections caused by HIV-1, HBV, and herpes simplex virus. The present invention also includes pharmaceutical compositions comprising a compound of Formula I and a suitable pharmaceutical carrier.

The compounds are taught to work via attachment to cell membranes and thus are particularly effective against infections caused by membrane-containing or envelope-containing viruses (col. 9, lines 42-45). While Kucera *et al.* exemplify the treatment of HIV-1 infections, the inventors state that the compounds of Formula I can also be used to treat the instantly claimed respiratory syncytial virus infections (col. 9, lines 56-61). With respect to claim 39, which recites modes of administration, Kucera *et al.* teach the same modes of administration (col. 10, lines 14-21).

The presently amended claims differ from Kucera *et al.* in that the claimed compounds are now limited to compounds wherein R_1 is $-\text{NHC}(\text{O})\text{C}_{11}$ alkyl; R_2 is $-\text{OX}$, where X is ethyl; and R_3 is phosphocholine. In the compounds disclosed in Kucera *et al.*, $\text{X}-\text{R}_1$ corresponds to the claimed $-\text{NHC}(\text{O})\text{C}_{11}$ alkyl substituent; $-\text{Y}-\text{R}_2$, wherein Y is O and R_2 is a branched or unbranched, saturated or unsaturated C_6 to C_{14} alkyl group corresponds to the $-\text{OCH}_2\text{CH}_3$ substituent; and when R_6 is ethyl and R_3 , R_4 , and R_5 are methyl corresponds to the claimed phosphocholine. The instantly claimed compounds thus differ from the genus of compounds disclosed in Kucera only in the length of the R_2 alkyl chain. Whereas Kucera *et al.* disclose that

Art Unit: 1614

the R₂ alkyl chain can be from C₆ to C₁₄ alkyl group, the instantly claimed compounds comprise a C₂ alkyl group.

Kucera *et al.* clearly suggest that the length of attached alkyl groups can be modified and still elicit functional antiviral compounds. For examples, compounds wherein R₂ is C₈, C₁₀, and C₁₂ were all demonstrated to have antiviral activity (Table 1). The courts have held that “structural similarity between claimed and prior art subject matter, proved by combining references or otherwise, where the prior art gives reason or motivation to make the claimed compositions, creates a prima facie case of obviousness.” *Dillon*, 919 F.2d at 692. In addition to structural similarity between the compounds, a prima facie case of obviousness also requires a showing of “adequate support in the prior art” for the change in structure. *In re Grabiak*, 769 F.2d 729, 731-32 [226 USPQ 870] (Fed. Cir. 1985).

The court elaborated on this requirement in the case of *In re Deuel*, 51 F.3d 1552, 1558 [34 USPQ2d 1210] (Fed. Cir. 1995), where the court stated that “[n]ormally a prima facie case of obviousness is based upon structural similarity, *i.e.*, an established structural relationship between a prior art compound and the claimed compound.” That is so because close or established “[s]tructural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds.” *Id.* A known compound may suggest its homolog, analog, or isomer because such compounds “often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.” *Id.*

In the instant case, Applicant’s compounds differ from Kucera’s compounds in that the claimed compounds are merely homologs of those disclosed in Kucera (*i.e.*, the claimed compounds only differ in the length of the alkyl chain attached at the R₂ position of the Kucera compounds. Kucera discloses branched or unbranched, saturated or unsaturated C₆ to C₁₄ alkyl groups whereas the instantly claimed compounds comprise a C₂ alkyl group. However, in light of the fact that Kucera clearly contemplates that the alkyl groups attached to the R₂ position can vary greatly (from C₆ to C₁₄ carbons) and further in view of the fact that compounds with differing alkyl chain lengths all possess antiviral activity, one skilled in the art would have found it obvious that a compound having chain length of C₂ carbons would also possess antiviral activity.

Art Unit: 1614

In support of the above findings, the Examiner additionally cites Kucera *et al.* ('584) who disclose methods of treating hepatitis virus infections comprising administering compounds of Formula I, which compounds are structurally related to the claimed compounds and those disclosed in Kucera *et al.* ('437) (see col. 1, line 60 to col. 2, line 48). See also compounds CP-49 and CP-51 in Example 6, which are phospholipid compounds as recited in the instant claims wherein R₂ -CH₂CH₃. These compounds were demonstrated to have anti-HBV activity. Compare to Kucera *et al.* ('437), wherein compound CP-128 (R₂ is C₁₀) disclosed therein is also demonstrated to have anti-HBV activity (Example 9).

Accordingly, the instantly claimed methods of treating RSV infections comprising administering a compound of Formula I would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. Kucera *et al.* ('437) clearly motivate one skilled in the art to use compounds of Formula I to treat viral infections and even teach that respiratory syncytial virus infections are a type of infection that may be treated with the compounds of the invention. Kucera *et al.* ('584) is provided as evidence that compounds having lower alkyl groups in the R₂ position maintain antiviral activity. As such, one skilled in the art would have been imbued with at least a reasonable expectation that the compounds of Formula I as taught in Kucera *et al.* ('437) having a C₂ alkyl group in the R₂ position would also be effective at treating viral infections, including the instantly claimed RSV, as evidenced by Kucera *et al.* ('584).

Response to Arguments

Applicants' arguments have been carefully considered but they are not deemed persuasive. Applicants argue that the claims have been amended to recite methods for treating a host with RSV comprising administering to a host in need thereof an anti-RSV effective amount of two specific compounds: 3-dodecanamido-2-ethoxypropyl-1-phosphocholine and 3-decanamido-2-ethoxypropyl-1-phosphocholine. Applicants assert that Kucera does not disclose or suggest the two compounds recited in the amended claims. In support of this argument, Applicants state that the fact that Kucera I discloses the R₂ as a C₆-C₁₈ alkyl group would not motivate one of ordinary skill in the art to include an ethyl group as recited in the instant claims. Rather, Applicants allege that the requirement of R₂ group as a C₆-C₁₈ alkyl group in Kucera I

Art Unit: 1614

teaches away from the ethyl group in the instant claims because the skilled artisan “would not explore the possibility of the lower alkyl groups at R₂ position”.

In response, the Examiner respectfully submits that Kucera II provides the requisite teaching and suggestion to modify the compounds of Kucera I to employ lower alkyl groups at the R₂ position. In this regard, as discussed above compounds CP-49 and CP-51 in Example 6 of Kucera II, are phospholipid compounds as recited in the instant claims wherein R₂ -CH₂CH₃. These compounds were demonstrated to have anti-HBV activity. Compare to Kucera I, wherein compound CP-128 (R₂ is C₁₀) disclosed therein is also demonstrated to have anti-HBV activity (Example 9). While Kucera II does not disclose the treatment of RSV, Kucera I generally discloses the treatment of virus infections, including hepatitis viral infection (as also explicitly disclosed in Kucera II) and RSV. Given the proven efficacy of compounds of both Kucera I and Kucera II in treating HBV infections, wherein such compounds have alkyl groups ranging from C₁ to C₁₀ alkyl, the skilled artisan would reasonably expect the instant claimed compounds to also be effective to treat RSV.

Regarding the Kucera II reference, Applicants argue that Kucera II fails to remedy the deficiency of Kucera I because Kucera II is directed to the treatment of hepatitis infections, not RSV. Applicants argue that a skilled artisan would not be motivated to modify the compounds indicated for the treatment of hepatitis for the treatment of a different unrelated virus (RSV). In response, the Examiner respectfully submits that it is the combination of the cited prior art that teaches, suggests, and motivates the claimed treatment of RSV with the claimed compounds. Kucera I discloses the treatment of viral infections, including hepatitis and RSV infections, with compounds structurally related to the claimed compounds. The differences between the compounds disclosed in Kucera I and those recited in the instant claims are discussed at length *supra*. Kucera II discloses compounds also structurally related to both the claimed compounds and those disclosed in Kucera I. While it is true that the disclosure of Kucera II is limited to the treatment of hepatitis infections, Kucera II provides factual evidence that the length of the alkyl chain at the R₂ position of the Kucera I has minimal effect on the antiviral activity of the compounds. Because compounds having an ethyl group in the R₂ position have anti-HBV activity (as evidenced by Kucera II) and compounds having a longer chain length (C₁₀) at the R₂ position maintain this anti-HBV activity (as evidenced by Kucera I), the skilled artisan would

Art Unit: 1614

have predicted that the claimed compounds would be effective antiviral compounds. Kucera I suggests the treatment of the claimed viral infection (RSV) and the combination of Kucera I and Kucera II would motivate the skilled artisan to try phospholipid compounds having different alkyl group chain lengths for the treatment of viral infections. Applicants have presented no factual evidence that the claimed compounds demonstrate unexpected anti-RSV activity that other phospholipid compounds suggested and motivated by combined teachings of Kucera I and Kucera II do not possess.

Accordingly, the rejection of claims 1-2, 6-8, and 39 is maintained for the reasons of record and as reiterated above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

March 16, 2010

Application/Control Number: 10/781,894

Page 9

Art Unit: 1614